CLAIMS

We claim:

1. An antibody comprising the amino acid sequence as set out in SEQ ID NO:19, SEQ ID NO:25, SEQ ID NO:31, SEQ ID NO:37, or SEQ ID NO:52.

2. Then antibody of claim 1, comprising an amino acid sequence substantially as set out in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:47, or SEQ ID NO: 49.

3. The antibody of claim 1, comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:47, and SEQ ID NO:49.

4. The antibody of claim 1, wherein the antibody specifically binds to an amino acid sequence that is at least 95% identical to any sequence of at least 100 of contiguous amino acids of at least one sequence selected from group consisting of SEQ ID NO:41 and SEQ ID NO:56.

5. The antibody of claim 1, wherein the antibody specifically binds to the extracellular domain of PD-1 with an affinity constant greater than 10^7 M^{-1}.

6. The antibody of claim 4, where the antibody inhibits the binding of PD-L to PD-1 with an IC_{50} of less than 10 nM.

7. The antibody of claim 1, wherein the antibody is human.

8. The antibody of claim 1, wherein the antibody is IgG_1 or IgG_4.

9. The antibody of claim 8, wherein the antibody is $IgG_{1\lambda}$ or $IgG_{1\kappa}$.

10. The antibody of claim 1, wherein the antibody is PD1-17, PD1-28, PD1-33, PD1-35, or PD1-F2.

11. A pharmaceutical composition comprising the antibody of claim 1.

12. A method of treatment comprising administering an effective dose of the pharmaceutical composition of claim 11.

13. The method of claim 12, wherein the pharmaceutical composition is administered to a subject in need for treatment or prevention of a disorder selected from the group consisting of an autoimmune disorder, an immune response to a graft, an allergic reaction, and cancer.

14. The method of claim 12, wherein the subject is a human.

15. An antibody comprising human framework regions and means for specific binding to PD-1, wherein the antibody is capable of blocking binding between PD-1 and PD-L1.

16. The antibody of claim 15, wherein the means comprises a CDR derived from PD1-17, PD1-28, PD1-33, PD1-35, or PD1-F2.

17. An isolated nucleic acid encoding the antibody of claim 1.

18. An expression vector comprising the nucleic acid of claim 17.

19. A host cell comprising the vector of claim 18.

20. The host cell of claim 19, wherein the host cell is chosen from: an *E. Coli* bacterium, a Chinese hamster ovary cell, a HeLa cell, and a NS0 cell.

21. The nucleic acid of claim 17, wherein the nucleic acid encodes the amino acid sequence set out in SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:47, or SEQ ID NO:49.

22. The nucleic acid of claim 21, wherein the nucleic acid comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:46, and SEQ ID NO:48.

23. A method of making an antibody that specifically binds with PD-1, the method comprises:

(a) providing a starting repertoire of nucleic acids encoding a variable domain that either includes a CDR3 to be replaced or lacks a CDR3 encoding region;

(b) combining the repertoire with a donor nucleic acid encoding an amino acid sequence substantially as set out in SEQ ID NO:19, SEQ ID NO:25, SEQ ID NO:31, SEQ ID NO:37, or SEQ ID NO:52, such that the donor nucleic acid is inserted into the CDR3 region in the repertoire, so as to provide a product repertoire of nucleic acids encoding a variable domain;

(c) expressing the nucleic acids of the product repertoire;

(d) selecting an antigen-binding fragment specific for PD-1; and

(e) recovering the specific antigen-binding fragment or nucleic acid encoding the binding fragment.

24. An antibody produced by the method of claim 23.

25. A method of modulating adaptive immune response comprising contacting a lymphocyte with an anti-PD-1 antibody.

26. The method of claim 25, wherein the lymphocyte is a T cell, B cell, or monocyte.

27. The method of claim 25, wherein the antibody is as in claim 1.

28. The method of claim 25, wherein the antibody is as in claim 24.

29. The method of claim 25, wherein the antibody is immobilized on a support matrix or crosslinked.

30. The method of claim 25, wherein the support matrix comprises one or more material chosen from agarose, dextran, cellulose, PVDF, silica, nylon, dacron, polystyrene, polyacrylates, polyvinyls, teflons, polyglycolic acid, polyhydroxyalkanoate, collagen, and gelatin.

31. The method of claim 25, wherein the anti-PD-1 antibody modulates immune cell response mediated by an antigen receptor.

32. The method of claim 31, wherein the antigen receptor signal is co-presented with the anti-PD-1 antibody.

33. The method of claim 31, wherein the antigen receptor signal and anti-PD-1 antibody are spaced by no more than 100 μm.

34. The method of claim 31, wherein the antigen receptor signal is delivered by an anti-CD3 antibody.